(automobile spray paint, laminates). Physicians need to be alert to the possibility that "strange" causes of asthma may lurk in increasingly complex workplaces.

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Bronchoscopy and Lasers

Fluorescence bronchoscopy is a sensitive method to locate small mucosal or intrabronchial cancer lesions not found on routine bronchoscopy in patients with positive sputum cytology studies and normal findings on chest x-ray films. Diagnosis is warranted at this early stage (stage 0, or $T_{IS}N_0M_0$) because resection may be expected to be 90% to 100% curative. With this method hematoporphyrin derivative, which is retained within cancer cells (of all histologic types, primary or metastatic), is injected intravenously. The fluorescence bronchoscope uses violet light (410 nm) from a krypton ion laser, conducted via a fine quartz fiber (0.4 nm) in its suction channel, to its tip. Fluorescing lesions are visualized with an image intensifier, are then brushed and a forceps biopsy done for specific diagnosis.

Photoradiation therapy for endobronchial tumors by bronchoscopy uses the photodynamic action of hematoporphyrin derivative within tumor cells to produce singlet oxygen when activated by red light (630 nm) conducted via a quartz fiber from an argon-pumped dye laser. Power is low (200 mW), and there is no immediate visible change or coagulating effect. Cell and cell membrane function are gradually impaired so that tumor cells die over the next 24 to 48 hours. Tumor debris is then removed by repeat-bronchoscopy, to open up the bronchus to its full extent. Even a totally occluded bronchus can be fully opened up, and an atelectatic lung, lobe or segment may be re-aerated. Methods of light application developed are effective and efficient; generally (80% to 90% of cases) only one treatment is required. There have been no complications during photoradiation treatment of obstructing endobronchial tumors. Photoradiation therapy for early bronchial cancer is potentially curative, and clinical trials are under way.

Photocoagulation therapy uses pulses of a beam of intense (20 to 40 W) infrared light (1,060 nm) from an Nd-YAG laser. Tumor tissue is thereby immediately coagulated by heating (50°C to 60°C), or can be vaporized (100°C) by higher power (40 to 90 W). Large obstructing tracheal and main bronchus tumors after coagulation can be sheared off by the tip of the rigid bronchoscope. Tumors and granulation tissue masses and fibrotic stenotic areas caused by an endotracheal tube or tracheostomy can be vaporized. The tip of the fiber must be carefully aimed to prevent penetration of the wall, hemorrhage and possible death.

These new advances in bronchoscopic laser therapy are effective and safe in experienced hands. Still to be documented are patient benefits in terms of survival, the duration of control of the tracheobronchial lesions and whether they recur, the degree of improved breathing and lessened cough and the prevention of recurrent respiratory tract infections and distal pneumonia.

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Drug Therapy for Pulmonary Hypertension

THE TREATMENT of pulmonary hypertension depends on its cause and includes such diverse measures as anticoagulant or fibrinolytic therapy for pulmonary embolic disease; oxygen, bronchodilators and pulmonary hygiene for patients with chronic obstructive pulmonary disease, and surgical treatment for patients with congenital heart disease and mitral stenosis. There is some evidence that the use of the bronchodilator terbutaline sulfate may decrease pulmonary vascular resistance and lessen the load of the right ventricle in patients with chronic obstructive pulmonary disease.

A variety of vasodilator drugs have been used with varying success in the treatment of primary pulmonary hypertension and other forms of pulmonary hypertension. These include tolazoline hydrochloride (25 mg every four to six hours), isoproterenol hydrochloride (10 to 20 mg sublingually every three to four hours), hydralazine hydrochloride (25 to 75 mg every six hours), diazoxide (100 to 200 mg every 8 to 12 hours) and, most recently, nifedipine (10 to 40 mg every six hours). Individual patient response is influenced by the summation of pharmacologic effects on the systemic and pulmonary circulations. These vary from person to person. Vasodilators may reduce pulmonary vascular resistance and pulmonary artery pressure may not change if the cardiac output increases as the pulmonary vascular resistance falls.

Alternatively, pulmonary artery pressure may increase in patients in whom systemic effects predominate, resulting in a fall in systemic vascular resistance and increased cardiac output without a simultaneous fall in pulmonary vascular resistance. Initiation of therapy for primary pulmonary hypertension requires heart catheterization and the careful hemodynamic assessment of individual patient response to specific drugs.

Total heart-lung transplantation has been successfully completed in victims of primary pulmonary hypertension and is an experimental form of treatment that holds promise.

To develop a better understanding of the natural history, pathophysiology and response to therapy of

primary pulmonary hypertension, a national registry of cases and a cooperative, multicenter study group has been established. Information regarding referral of patients into the study may be obtained by writing to Primary Pulmonary Hypertension Registry, c/o Chief, Interstitial Lung Disease Branch, Division of Lung Diseases, National Heart, Lung and Blood Institute, Westwood Bldg, 6A03, 5333 Westbard Avenue, Bethesda, MD 20205.

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Staging of Lung Cancer

IN VIEW OF variations in published survivorship data for patients with lung cancer with regional nodal involvement—that is, hilar-mediastinal—advances in prethoracotomy diagnostic techniques and the lack of uniformly accepted anatomic definitions of each regional-pulmonary nodal station, the American Thoracic Society formed a committee on lung cancer and charged it to:

- Develop a map of regional pulmonary lymph nodes that would be acceptable to all physicians who care for patients with lung cancer.
- Develop multifactorial criteria for the extent, degree and type of nodal involvement in cases of primary lung cancer.

The recommendations of this committee, with respect to these two charges, were recently published. A map of regional pulmonary nodes was presented and the anatomic definitions of each nodal station were tabulated. It was recommended that this mapping technique be adopted to ensure uniformity in recording and publishing patient data. Only then can surgical series be compared and the impact on five-year survival determined. Such prospective data may allow clearer definition in the future of the criteria for surgical resection.

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Nonsurgical Treatments for Sleep Apnea Syndromes

SLEEP APNEA SYNDROMES involve a complex of manifestations that often interact progressively, threatening a patient's comfort, functioning and occasionally life. Such features include sleep fragmentation, autonomic nervous system stimulation, cardiovascular changes and pulmonary dysfunction. A thorough medical evaluation, including imaging of the upper airway, is necessary to determine the efficacy of treatment, the evaluation being directed at part or all of such perturbations, carefully defining the importance of local anatomic abnormalities and of central or effector system impairment.

Approaches to managing sleep apnea syndromes have included surgical and mechanical corrections (not considered in this article), oxygen therapy, weight reduction where appropriate and the use of a variety of medications. Evaluation has been applied to at least the following medicines:

- Clomipramine hydrochloride,
- Protriptyline hydrochloride,
- Medroxyprogesterone acetate,
- Acetazolamide,
- L-Tryptophan,
- Theophylline ethylenediamine (aminophylline),
- Naloxone hydrochloride,
- Bromocriptine mesylate,
- Strychnine,
- Almitrine.

Conclusions concerning efficacy may be broadly divided into those with predominantly central (or diaphragmatic) or predominantly obstructive causes.

1. No one has reported that drugs alone have completely resolved a severe obstructive or central syndrome in which apnea is continuous and associated with significant repetitive oxygen desaturation during sleep.

2. Weight loss alone in obese persons has led to the disappearance of a predominantly central or a predominantly obstructive sleep apnea syndrome in specific, selected cases. Low-flow oxygen given during sleep in conjunction with weight loss, again in selected cases, particularly in predominantly central or mixed syndromes, has helped to halt significant oxygen desaturation during the weight loss period.

3. Some drugs have essentially no effect, such as bromocriptine (given for obstructive apnea), naloxone (for obstructive apnea; reports conflict regarding predominantly central problems but even in these cases most results are negative) and almitrine (for obstructive apnea).

4. Other drugs have been beneficial *in certain cases.* Aminophylline has been helpful in treating central apnea associated with cardiac failure. (In only one article is central apnea clearly distinguished from the Cheyne-Stokes breathing pattern, which is also alleviated by aminophylline). Strychnine has been reported effective in non-rapid-eye-movement (NREM) sleep apnea, but it has only been tried in three patients. Acetazolamide is helpful in treating central sleep apnea at high altitudes, but its efficacy in cases of central apnea at sea level is questioned. L-Tryptophan, which also affects sleep, has been helpful when taken in 3- to 5-gram doses before bedtime in mild or moderate central and mixed apnea syndrome, particularly in the elderly. The tricyclic medications (initially clomipramine, more recently protriptyline) have been reported effective in mild to moderate central, mixed and obstructive syndromes since 1970. Presently protriptyline, 10 to 20 mg, is most commonly prescribed to be taken at bedtime. It affects muscle tone and rapid-eye-movement (REM) sleep, but the well-known tricyclic antidepressant side effects, particularly